

**Application No.: 10/572,404**  
**Filing Date: March 16, 2006**

## **REMARKS**

Claims 1-4, 6, 8-11, 13, and 15-17 have been cancelled. Claims 5, 7, 12, 14, 18 and 19 have been amended. New claims 20-22 are added. Claims 5, 7, 12, 14, and 18-22 are now pending in this application.

The claims have been amended to specify 9,19-cyclolanostan-3-ol or 24-methylene-9,19-cyclolanostan-3-ol in an amount of 0.001-10% by dry mass. Support is found in the present specification. See, for example page 9 first full paragraphs 1 and 2. Support for new claims 20-22 is found at page 17, 2<sup>nd</sup> full paragraph to page 18, line 6 and in Preparation Example 2 at pages 30-31. Accordingly, the amendments do not constitute the addition of new matter. Applicant respectfully requests the entry of the amendments and reconsideration of the application in view of the amendments and the following remarks.

### **Rejection under 35 U.S.C. § 101**

Claims 1-18 are rejected under 35 U.S.C. § 101 as directed to non-statutory subject matter.

The amended claims are directed to plant extracts which have been partially purified so as to contain the specified compounds, 9,19-cyclolanostan-3-ol or 24-methylene-9,19-cyclolanostan-3-ol in an amount of 0.001-10% by dry mass. Accordingly the present claims do not read upon natural products.

In view of Applicants' amendments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

### **Rejection under 35 U.S.C. § 112, second paragraph**

Claims 1-7 and 9 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding the use of the term "drug", Applicants clarify that the term "drug" has the usual and customary meaning in the art of a substance or preparation which has a physiological effect when ingested or otherwise introduced into the body.

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Regarding claim 19, the expression “or more” has been deleted so that it is now clear that the concentration of the compounds should be between “0.001 to 10% by dry mass”.

In view of Applicants’ amendments and arguments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

**Rejection under 35 U.S.C. § 112, first paragraph - scope of enablement**

Claims 1-19 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for compositions and methods comprising compounds wherein R4 is -OH or =O, does not reasonably provide enablement for compositions and methods comprising compounds wherein R4 is other than -OH or =O.

This ground of rejection is addressed by amendment of the claims to specify 9,19-cyclolanostan-3-ol or 24-methylene-9,19-cyclolanostan-3-ol. Support for the amendment is found in the present specification at page 9, first full paragraph.

In view of Applicants’ amendments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

**Rejection under 35 U.S.C. § 102(b)**

Claims 1-3, 8-10, 15, 16, and 18 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Yongchaiyudha, et al. (Phytomedicine 3(3): 241, 1996) as evidenced by Tanaka, et al. (Biol Pharm. Bull. 29(7): 1418, 2006).

This ground of rejection is moot with respect to claims 1-3, 8-10, and 15-16 which have been canceled.

Claim 18 has been amended to specify that the compound to be administered is “9,19-cyclolanostan-3-ol or 24-methylene-9,19-cyclolanostan-3-ol”. Support for the amendment is found in the present specification at page 9, first full paragraph.

Yongchaiyudha, et al. merely disclose administration of Aloe vera juice prepared from Aloe vera gel (page 242, col. 1 under “Sample”). Yongchaiyudha, et al. do not teach administration of 9,19-cyclolanostan-3-ol or 24-methylene-9,19-cyclolanostan-3-ol as claimed.

In view of Applicants’ amendments and arguments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

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**Rejection under 35 U.S.C. § 102(b)**

Claims 1-3, 8-10, 15, 16, and 18 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Abou Zeid (Egypt J. Phar. Sci. 39 (4-6): 379, 1988).

This ground of rejection is moot with respect to claims 1-3, 8-10, and 15-16 which have been canceled.

Claim 18 has been amended to specify that the compound to be administered is “9,19-cyclolanostan-3-ol or 24-methylene-9,19-cyclolanostan-3-ol”. Support for the amendment is found in the present specification at page 9, first full paragraph.

Abou Zeid teaches 24-methylene-cycloaltanol (24-methylene-9,19-cyclolanostan-3-ol) (page 392). Abou Zeid does not teach 9,19-cyclolanostan-3-ol.

Abou Zeid does not teach administration of 24-methylene-9,19-cyclolanostan-3-ol “to a subject whose hyperglycemia is to be improved” as claimed. While Table 5 teaches that hexane extracts of *M cavendishii* and *M. sapientum* lower blood glucose level, there is no disclosure that these extracts contain 24-methylene-9,19-cyclolanostan-3-ol in any amount or that 24-methylene-9,19-cyclolanostan-3-ol is the active component.

In view of Applicants’ amendments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

**Rejection under 35 U.S.C. § 103(a)**

Claims 4-7, 11-14, 17 and 19 are rejected under 35 U.S.C. § 103 (a) as being unpatentable over Yongchaiyudha, et al. (Phytomedicine 3(3): 241, 1996) as evidenced by Tanaka, et al. (Biol Pharm. Bull. 29(7): 1418, 2006).

This ground of rejection is moot with respect to claims 4, 6, 11, 13, and 17 which have been cancelled.

Present claims 5, 7, 12, 14, and 19 include the limitation that the organic solvent or hot water extract contains 0.001 to 10% by dry mass of 9,19-cyclolanostan-3-ol or 24-methylene-9,19-cyclolanostan-3-ol. The limitation that the extract contains 0.001 to 10% by dry mass is found in original claims 5 and 19.

On this point, the Examiner takes the position that the “although Yongchaiyudha, et al. do not expressly teach this, it is likely that the compositions taught by Yongchaiyudha, et al.,

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whether extract, gel, or juice, would naturally contain this concentration" (Office Action, page 9, paragraph 4).

In rebuttal, Applicants present the Declaration of Miyuki Tanaka (Tanaka Declaration), one of the inventors of the present application. In the Declaration, the content of 9,19-cyclolanostan-3-ol and 24-methylene-9,19-cyclolanostan-3-ol in a sample of Aloe vera juice manufactured according to Yongchaiyudha, et al. was determined by LC/MS/MS (item 6, of the Declaration, see (1)).

As shown in Table 1 on page 4 of the Tanaka Declaration (item 6 (6)), amounts of 9,19-cyclolanostan-3-ol and 24-methylene-9,19-cyclolanostan-3-ol were 0.000022% and 0.000016% by mass, respectively, much lower than claimed by Applicants.

Accordingly, Yongchaiyudha, et al. do not teach or suggest the claimed drug compositions. The Aloe vera juice extracts of Yongchaiyudha, et al. do not contain 0.001 to 10% by dry mass of 9,19-cyclolanostan-3-ol or 24-methylene-9,19-cyclolanostan-3-ol. Likewise, Yongchaiyudha, et al. do not teach or suggest a method of improving hyperglycemia by administering a plant extract containing 0.001 to 10% by dry mass of 9,19-cyclolanostan-3-ol or 24-methylene-9,19-cyclolanostan-3-ol as the claimed composition differs from the Aloe vera juice extracts taught by Yongchaiyudha, et al.

Furthermore, it was not predictable from Yongchaiyudha, et al. that administration of 0.001 to 10% by dry mass of 9,19-cyclolanostan-3-ol or 24-methylene-9,19-cyclolanostan-3-ol would be effective to relieve hyperglycemia as there is no disclosure in Yongchaiyudha, et al. of these specific components. There would be no apparent reason for one of ordinary skill in the art to prepare a drug composition containing 0.001 to 10% by dry mass of 9,19-cyclolanostan-3-ol or 24-methylene-9,19-cyclolanostan-3-ol based on Yongchaiyudha, et al.

In view of Applicants' amendments, arguments and the Tanaka Declaration, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

**Rejection under 35 U.S.C. § 103(a)**

Claims 4, 5, 11, 12, 17 and 19 are rejected under 35 U.S.C. § 103(a) as unpatentable over Abou Zeid (Egypt J. Phar. Sci. 39 (4-6): 379, 1988).

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This ground of rejection is moot with respect to claims 4, 11 and 17 which have been cancelled.

As mentioned above, Abou Zeid teaches 24-methylene-cycloaltanol (24-methylene-9,19-cyclolanostan-3-ol) (page 392), but do not teach 9,19-cyclolanostan-3-ol.

Applicants' extract is a partially purified extract obtained from a plant of the family *Liliaceae*. In contrast, Abou Zeid teaches organic solvent extracts from *M cavendishii* and *M. sapientum*. Clearly, a plant extract obtained from the family *Liliaceae* will have different components than an extract from either *M cavendishii* or *M. sapientum* which are in a different family (*Musaceae*). For example, the extracts of Abou Zeid apparently do not contain 9,19-cyclolanostan-3-ol.

Abou Zeid do not teach 9,19-cyclolanostan-3-ol and 24-methylene-9,19-cyclolanostan-3-ol at a concentration of 0.01 to 10% by dry mass from a plant of the family *Lilaceous*. It is not predictable from Abou Zeid that a plant of the family *Liliaceae* would contain 9,19-cyclolanostan-3-ol and 24-methylene-9,19-cyclolanostan-3-ol. There is no apparent reason to isolate 0.001 to 10% by dry mass of 9,19-cyclolanostan-3-ol or 24-methylene-9,19-cyclolanostan-3-ol from any plant based upon Abu Zeid. Abu Zeid do not teach or suggest the claimed invention. Accordingly, the claimed compositions of Applicants are non-obvious in view of Abou Zeid.

In view of Applicants' amendments and arguments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

#### **Rejection under 35 U.S.C. § 103(a)**

Claims 6, 7, 13 and 14 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Abou Zeid as applied to claims 4, 5, 11, 12, 17 and 19 above and further in view of Yongchaiyudha, et al.

The limitations of claims 6 and 13 have been incorporated into claims 5 and 12.

As discussed above, while both Abou Zeid and Yongchaiyudha, et al. teach plant extracts having the effect of lowering blood sugar, neither Abou Zeid nor Yongchaiyudha, et al. disclose either 9,19-cyclolanostan-3-ol or 24-methylene-9,19-cyclolanostan-3-ol as active ingredients. Abou Zeid does not teach 9,19-cyclolanostan-3-ol at all. Yongchaiyudha, et al. merely teach

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Aloe vera extracts which do not contain 9,19-cyclolanostan-3-ol or 24-methylene-9,19-cyclolanostan-3-ol at the claimed concentration of 0.01 to 10 % by dry mass as evidenced by the Tanaka Declaration discussed above.

Accordingly, one of ordinary skill in the art having the teachings of Abou Zeid and Yongchaiyudha, et al. before him/her could only conclude that both Aloe vera and plants of the Musaceae family contain some component(s) that lower blood sugar. One of ordinary skill in the art would not be led to extracting an *Aloe vera* plant to provide a composition containing 9,19-cyclolanostan-3-ol or 24-methylene-9,19-cyclolanostan-3-ol at a concentration of 0.01 to 10% by dry mass. One of ordinary skill in the art would not administer a composition having 0.001 to 10% by dry mass of 9,19-cyclolanostan-3-ol or 24-methylene-9,19-cyclolanostan-3-ol to a subject having a need to improve hyperglycemia based upon the teaching of Abou Zeid and Yongchaiyudha, et al. taken separately or together.

In view of Applicants' amendments and arguments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

#### **Double patenting**

Claims 1-17 are provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-19 of copending Application No. 11/577,301.

Applicants intend to cancel claims 1-19 from the copending application. Withdrawal of the rejection is respectfully requested.

#### **No Disclaimers or Disavowals**

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, the Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. The Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior

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prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that the Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

**Co-Pending Applications of Assignee**

Applicant wishes to draw to the Examiner's attention to the following co-pending applications of the present application's assignee.

Serial Number	Title	Filed
10/564,464	GLYCOSIDE HAVING 4-METHYLERGOST-7-ENOL SKELETON AND HYPERGLYCEMIA IMPROVING AGENT	01/12/06
10/572,099	DRUG AND FOOD OR DRINK FOR IMPROVING HYPERGLYCEMIA	03/16/06
10/573,564	DRUG AND METHOD FOR PROLIFERATING NATURAL KILLER CELLS	03/27/06
11/580,173	INTERLEUKIN-18 INDUCER	10/12/06
11/576,652	DRUG AND FOOD OR DRINK FOR IMPROVING PANCREATIC FUNCTIONS	04/04/07
11/576,676	DRUG AND FOOD OR DRINK FOR IMPROVING PANCREATIC FUNCTIONS	04/04/07
11/577,301	DRUG AND FOOD OR DRINK FOR IMPROVING PANCREATIC FUNCTIONS	04/13/07
11/815,428	ALOE VERA EXTRACT, METHOD OF PRODUCING ALOE VERA EXTRACT, AND HYPERGLYCEMIA IMPROVING AGENT	08/02/07
11/855032	INTERLEUKIN-6 SUPPRESSIVE AGENT	13-Sep-2007
11/913022	AGENT FOR INHIBITING VISCERAL FAT ACCUMULATION	29-Oct-2007
11/913758	AGENT FOR INHIBITING VISCERAL FAT ACCUMULATION	06-Nov-2007
11/916008	AGENT FOR IMPROVING INSULIN RESISTANCE	29-Nov-2007
11/917870	AGENT FOR IMPROVING INSULIN RESISTANCE	17-Dec-2007
12/064607	AGENT FOR IMPROVING INSULIN RESISTANCE	22-Feb-2008

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**CONCLUSION**

In view of Applicants' amendments to the claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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